LIST OF REFERENCES CITED BY APPLICANT (*Use several sheets if necessary*) PTO FORM 1449 - Supplemental	ATTY. DOCKET NO. 03678.0073.DVUS04	APPLICATION NO. 10/682,545
	APPLICANT Ward M. Peterson et al.	
	FILING DATE October 8, 2003	GROUP 1623

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	1.						
	2.						
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APPLICANT: Ward M. Peterson *et al.*	
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	2.	US 6,548,658 B2	04/15/03	*Yerxa*	536	26.22	11/20/01
	3.	US 6,555,675 B2	04/29/03	*Rideout et al.*	536	25.6	03/23/01
	4.	US 6,596,725 B2	07/22/03	*Peterson et al.*	514	256	01/30/01
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dw	6.	US 6,696,425 B2	02/24/04	*Yerxa et al.*	514	47	12/19/01

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dw	7.	International Preliminary Examination Report	10/01/2004	PCT	—	—		

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Spears

DIG-specific signal was detected using a chromophore reaction against the alkaline phosphatase, yielding purple/black staining. The tissues were also counterstained with nuclear fast red. The control sense probe (right) shows no specific labeling. Labeling with the anti-sense probe showed $P2Y_2$ receptor mRNA localization in scattered nuclei in the ganglion cell and inner nuclear layers and through the inner segment layer of photoreceptors. Strong labeling throughout the RPE was also detected, and in endothelial cells of the choroidal blood vessels.

Example 2. Effects of Synthetic $P2Y_2$ Agonist UP_4dC on Cloned Human $P2Y_2$ Receptors

The dinucleotide, [P^1-(uridine 5-)-P^4-(2'-deoxycytidine 5'-)tetraphosphate tetrasodium salt](UP_4dC) INS37217, was tested for its activity (potency, efficacy, and selectivity) at cloned human P2Y receptor subtypes, which were stably expressed in 1321N1 astrocytoma cells. Activity was assessed using two *in vitro* indices of cell activation: 1) mobilization of intracellular calcium stores, and 2) accumulation of [^{3}H]-inositol phosphates ([3H]-IP). UP_4dC was evaluated for activity in both assays against cells expressing the $P2Y_1$, $P2Y_2$, $P2Y_4$, or $P2Y_6$ receptors.

UTP and UP_4dC induced mobilization of cytosolic calcium in 1321N1 astrocytoma cells expressing human $P2Y_2$ (Figure 2) receptors with EC_{50} values of 0.22 μM and 0.8 μM, respectively. The calcium response to 100 μM UP_4dC was 100% of the maximal response to UTP at $P2Y_2$ receptors. In conclusion, UP_4dC is a full agonist for calcium mobilization at $P2Y_2$ receptors compared to UTP.

UTP and UP_4dC stimulated [^{3}H]-IP accumulation in 1321N1 cells expressing human $P2Y_2$ (Figure 3) receptors with an EC_{50} values of 1.1 and 2.2 μM, respectively. The inositol phosphate response to 100 μM UP_4dC was approximately that of the maximal response to UTP. In conclusion, UP_4dC is a full agonist for inositol phosphate release at $P2Y_2$ receptors compared to UTP in the test system.

Example 3. UP_4dC Stimulates Fluid Absorption in Freshly Isolated RPE Monolayers

Fluid transport across freshly isolated, intact bovine and human fetal RPE monolayers was studied using a modified capacitance probe technique (Frambach, *et al.*, *Biophys. J.* 47(4):547-52 (1985); Hughes, *et al.*, *J Gen. Physiol.* 83(6):875-99 (1984)).

The RPE was mounted vertically in a modified Ussing chamber such that apical and